Using RGD to analyze genes associated with obesity

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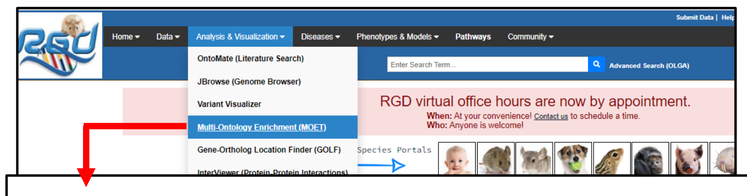
Abstract

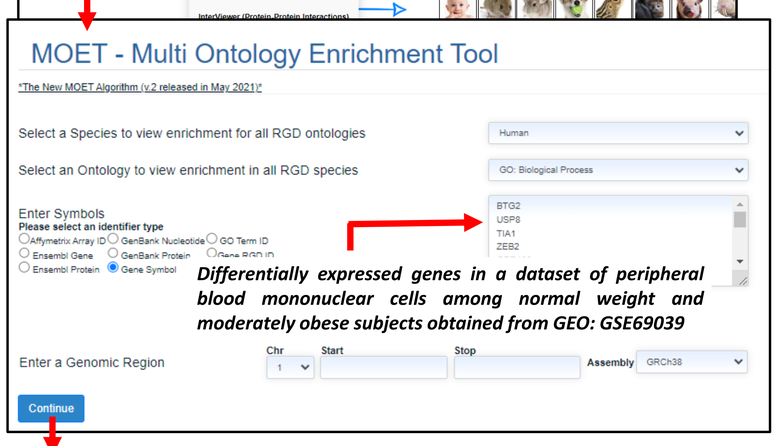
RGD (***https://rgd.mcw.edu***) provides a rich core of human genomic and phenotypic data with an infrastructure of standardized ontologies, Disease Portals, and many bioinformatics tools to allow users to explore and make disease-related connections among these datasets. These tools and data are integrated with nine other species used as models for human disease (rat, mouse, pig, chinchilla, dog, bonobo, 13-lined ground squirrel, vervet, and naked mole-rat) for translational research.

Obesity is a complex disease and a worldwide health concern due to its implication as a critical risk factor in multiple conditions, including stroke, dementia and COVID-19. As an example workflow, we used RGD's Multi-Ontology Enrichment Tool (MOET) to do an enrichment analysis of the top 200 differentially expressed genes in a gene expression profile dataset of peripheral blood mononuclear cells among normal weight and moderately obese subjects obtained from GEO (GSE69039). The top terms in biological process and pathway ontologies were cellular response to stress and regulatory pathway. The top term in the gene-chemical interactions (ChEBI) ontology was an antirheumatic drug which is interestingly associated with weight loss. To further analyze these genes, users can easily navigate from MOET to the other RGD tools such as Variant Visualizer to investigate clinical variants and GViewer for a genome-wide view of the genes.

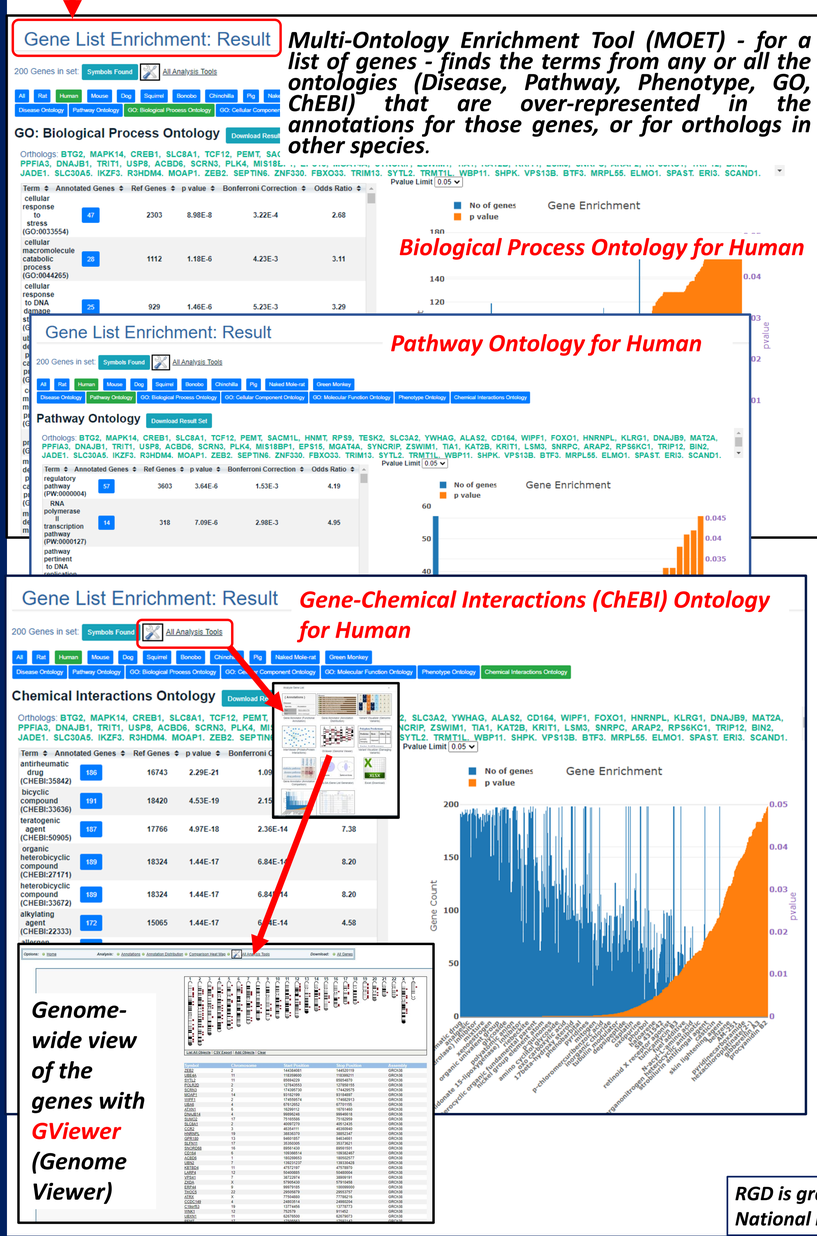
RGD provides researchers with the Obesity & Metabolic Syndrome Disease Portal as one of fifteen Disease Portals that offer data for genes, QTLs and rat strains associated with the disease. As another example, we generated a list of human genes common between obesity and stroke using the Obesity & Metabolic Syndrome Disease Portal and Object List Generator and Analyzer (OLGA). This list was used as input for the Variant Visualizer, which found the *LDLR* gene to include many predicted damaging variants and was also linked to Hypercholesterolemia. Additional information about the *LDLR* gene can be found on the RGD gene report page, including disease annotations, clinical variants with associated conditions, and links to the gene report pages of other RGD species. The rat *Ldlr* gene report page shows the multiple *Ldlr* rat strain genetic models available for obesity and obesity-related conditions research. For example, the SD-*Ldlr*^{em1Sage} strain page shows obesity-related disease and mammalian phenotype annotations and PhenoMiner (quantitative phenotype) data. In conclusion, RGD aims to build functionality to support widespread use and assist researchers in finding and utilizing the data and models they need to explore to further gene-to-disease research.

Explore gene list from external data resource (GEO)





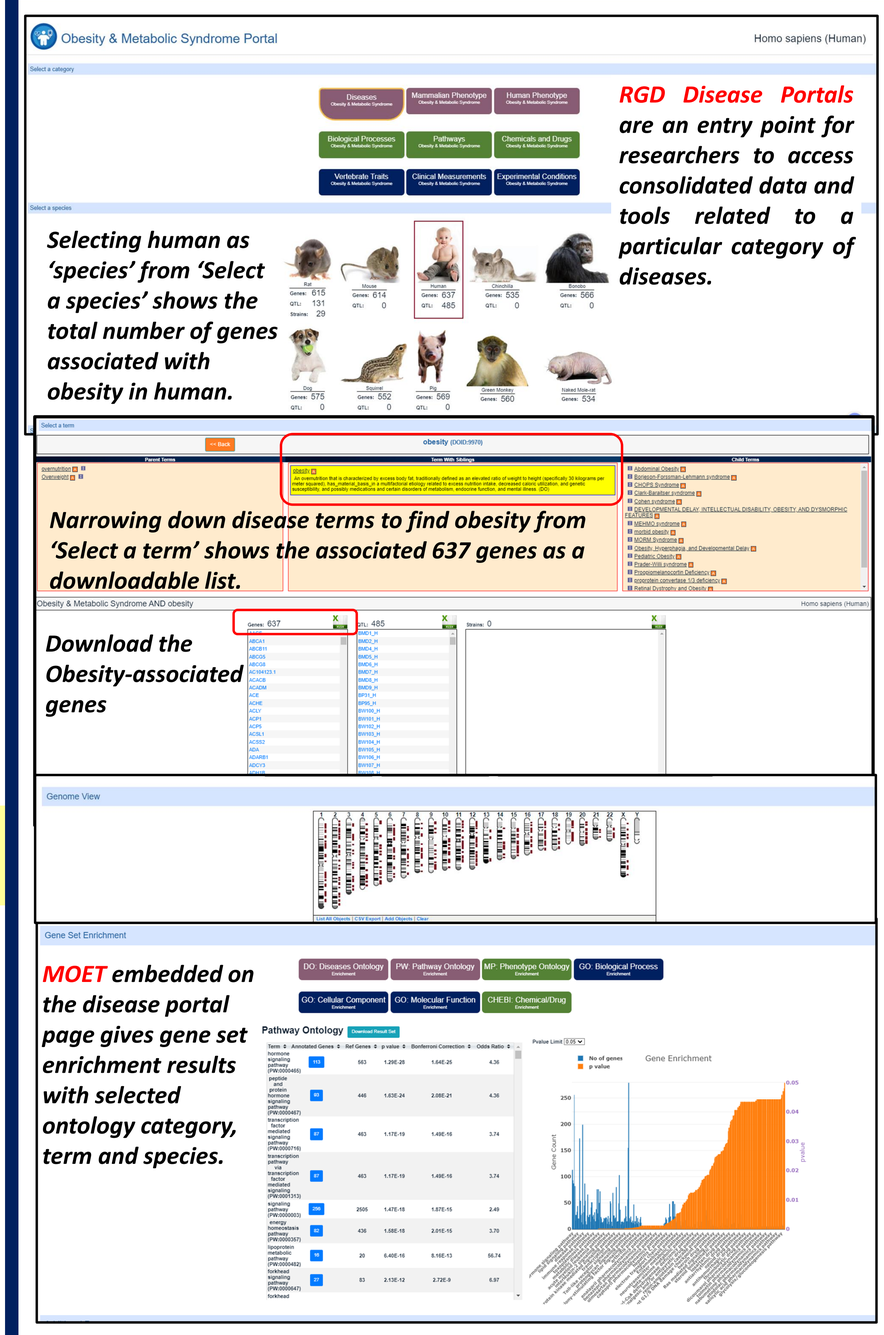
Differentially expressed genes in a dataset of peripheral blood mononuclear cells among normal weight and moderately obese subjects obtained from GEO: GSE69039



Multi-Ontology Enrichment Tool (MOET) - for a list of genes - finds the terms from any or all the ontologies (Disease, Pathway, Phenotype, GO, ChEBI) that are over-represented in the annotations for those genes, or for orthologs in other species.

Genome-wide view of the genes with GViewer (Genome Viewer)

Explore gene list from the RGD Obesity & Metabolic Syndrome Portal



RGD Disease Portals are an entry point for researchers to access consolidated data and tools related to a particular category of diseases.

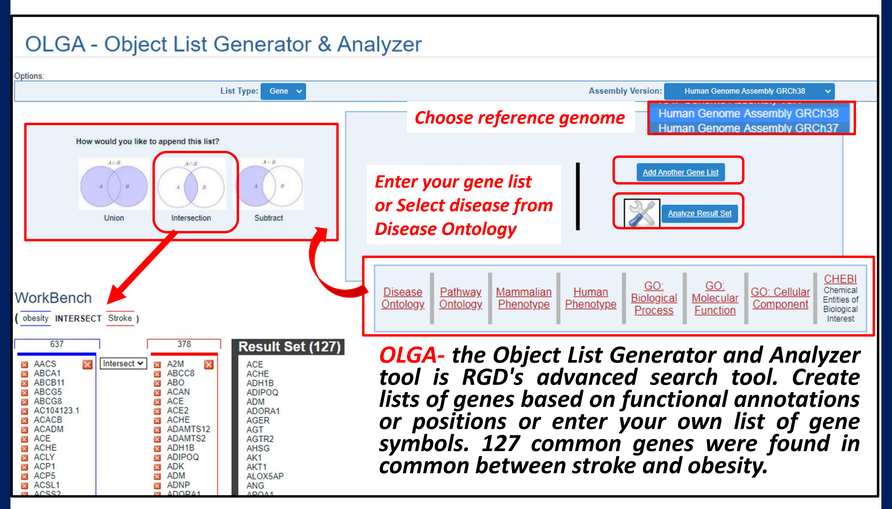
Selecting human as 'species' from 'Select a species' shows the total number of genes associated with obesity in human.

Narrowing down disease terms to find obesity from 'Select a term' shows the associated 637 genes as a downloadable list.

Download the Obesity-associated genes

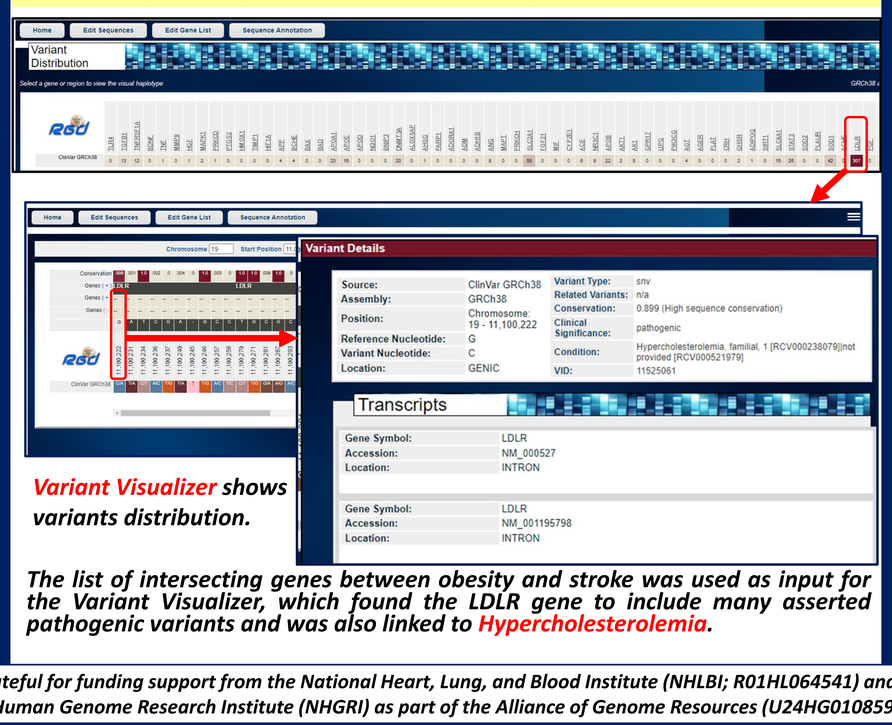
MOET embedded on the disease portal page gives gene set enrichment results with selected ontology category, term and species.

Find genes in common between Obesity and Stroke



OLGA- the Object List Generator and Analyzer tool is RGD's advanced search tool. Create lists of genes based on functional annotations or positions or enter your own list of gene symbols. 127 common genes were found in common between stroke and obesity.

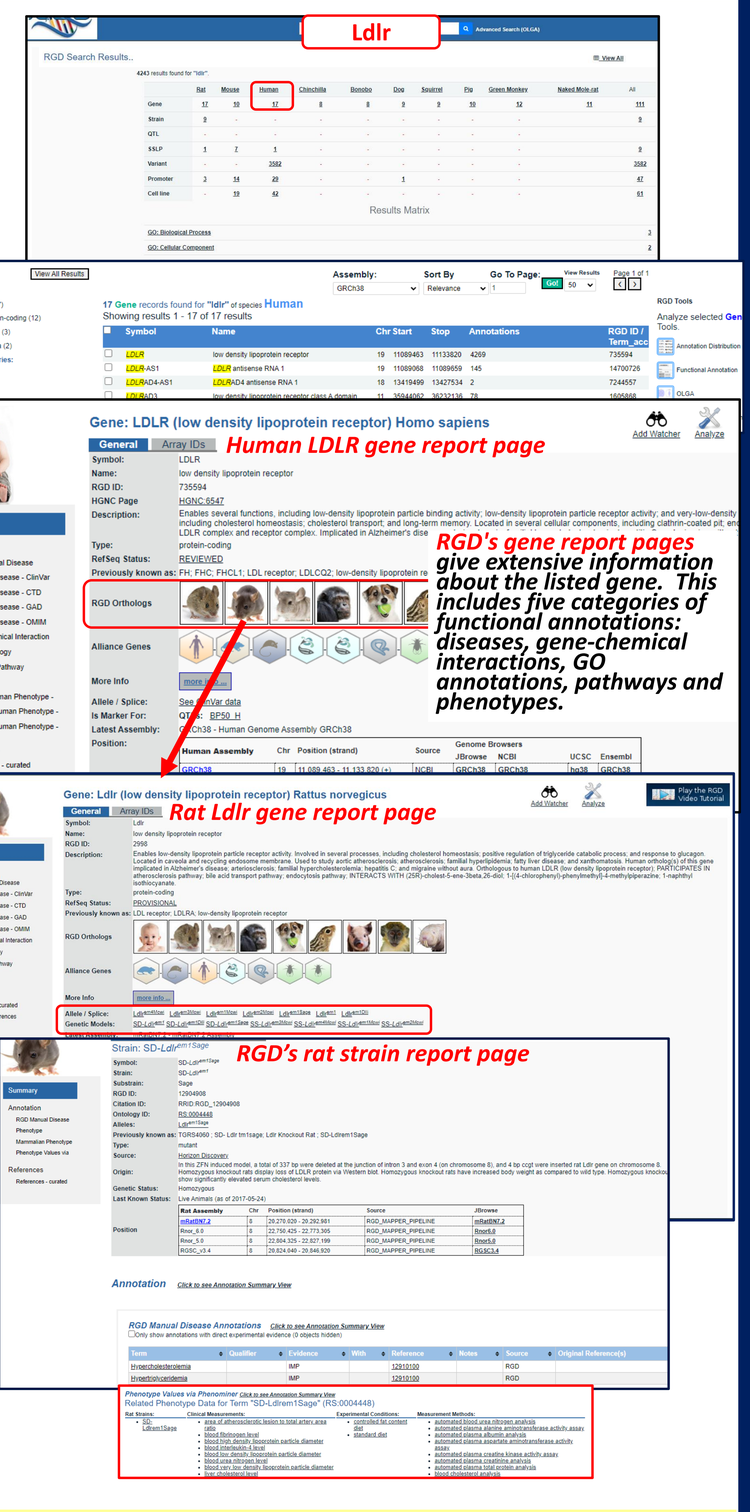
Find pathogenic variants using Variant Visualizer



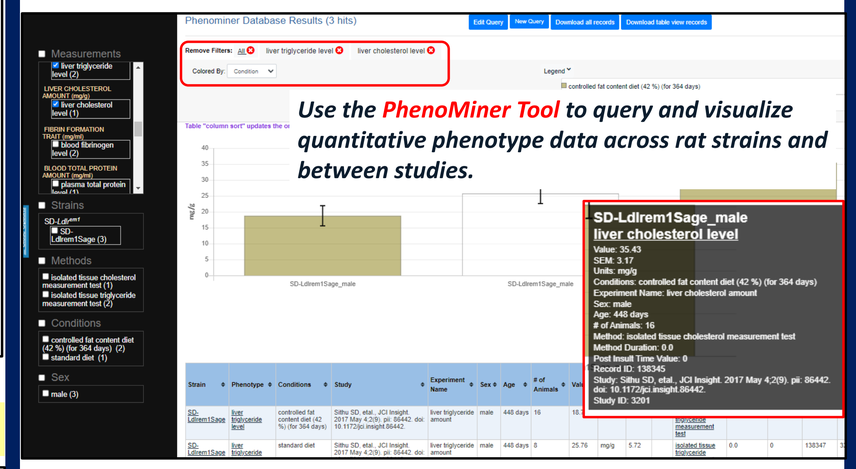
Variant Visualizer shows variants distribution.

The list of intersecting genes between obesity and stroke was used as input for the Variant Visualizer, which found the LDLR gene to include many asserted pathogenic variants and was also linked to Hypercholesterolemia.

Find genetic research models at RGD

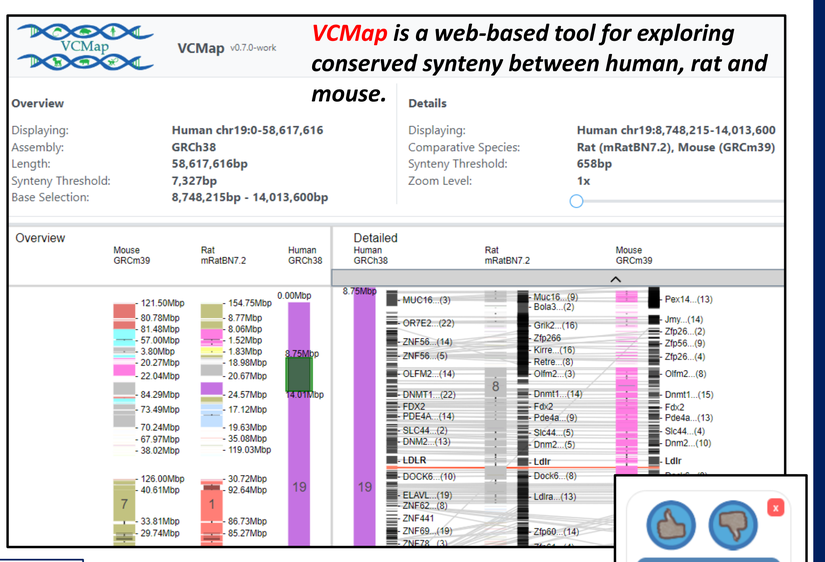


Compare quantitative phenotype data with PhenoMiner



Use the PhenoMiner Tool to query and visualize quantitative phenotype data across rat strains and between studies.

Visualize synteny with VCMap



VCMap is a web-based tool for exploring conserved synteny between human, rat and mouse.

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